REMARKS

In the Office Action dated February 24, 2004, Claims 25-26 and 29-32 are rejected under 35 U.S.C. §101 as allegedly drawn to non-statutory subject matter. Claims 25-26 and 29-32 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to satisfy the written description requirement. Claims 25-26 and 29-32 are also rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to satisfy the enablement requirement. Claims 25-26, 29 and 32 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gorman et al. (EP 0 260 148 A2). Claims 25 and 32 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Jiang et al. (*Gene* 185: 285-290, 1997). Claims 25 and 32 are rejected under 35 U.S.C. §102 (b) as allegedly anticipated by Blanchard et al. (*Biology of Reproduction* 56: 495-500, 1997). Claims 30 and 32 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gorman et al. (EP 0 260 148 A2) in view of Meulien (U.S. 5,521,070). Claims 30 and 32 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gorman (EP 0 260 148 A2) in view of Ciotti et al. (*Biochemistry* 35: 10119-10124, 1996).

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Claims 25-26 and 29-32 are rejected under 35 U.S.C. §101 as allegedly drawn to non-statutory subject matter.

It is observed that claims 25-26 and 29-31 are directed to a Sertoli cell comprising a vector. The Examiner states that the claims encompass a genetically modified Sertoli cell in a human, which is a non-statutory subject matter. The Examiner further states that claim 32,

directed to a genetically modified Sertoli cell isolated from a transgenic animal which encompasses a transgenic human, constitutes a non-statutory subject matter.

In response, Applicants have amended the claims 25-26 and 29-31 to recite an "isolated" Sertoli cell. Applicants have also amended claim 32 to recite "non-human transgenic animal". As such, it is respectfully submitted that the rejection of the claims under 35 U.S.C. §101 is overcome. Withdrawal of the rejection is respectfully submitted.

Claims 25-26 and 29-32 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges that the specification does not provide any description for any vector comprising a coding sequence for any non-protein compound that is necessary for cellular metabolism and homeostasis, or any genetically modified Sertoli cell comprising the same vector.

Claims 25-26 and 29-32 are also rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled. The Examiner alleges that the specification does not reasonably provide enablement for a genetically modified Sertoli cell comprising a vector comprising a coding sequence for a non-protein biological factor or the same isolated from a transgenic human.

In response, Applicants have amended claims 25-26 and 29-32 to recite a "biological protein". Support for this amendment is found in the specification, e.g., at page 8, line 8. In view of the amendment, Applicants respectfully submit that the rejections of the claims under the written description and enablement requirements of 35 U.S.C. §112, first paragraph, are overcome. Withdrawal of the rejections is respectfully submitted.

Claims 25-26, 29 and 32 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gorman et al. (EP 0 260 148 A2). The Examiner contends that Gorman et al. teach vectors and mouse Sertoli cells (TM4) that comprise the vectors. The Examiner indicates that the vectors disclosed in Gorman et al. include a promoter that functions in Sertoli cells and is operatively linked to a coding sequence for a desired heterologous protein (e.g., Factor VIII). The Examiner is of the opinion that the genetically modified Sertoli cells taught by Gorman et al. are inherently capable of creating an immunologically privileged site *in vivo*.

Claims 25 and 32 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Jiang et al. (*Gene* 185: 285-290, 1997). The Examiner contends that Jiang et al. teach primary rat Sertoli cells comprising a vector having a promoter which functions in Sertoli cells, operatively linked to a coding sequence for luciferase.

Claims 25 and 32 are rejected under 35 U.S.C. §102 (b) as allegedly anticipated by Blanchard et al. (*Biology of Reproduction* 56: 495-500, 1997). Blanchard et al. teach a recombinant adenovirus vector comprising a promoter (from the Rous sarcoma virus) operatively linked to a coding sequence for galactosidase (lacZ gene product), and rat Sertoli cells (both *in vitro* and *in vivo*) comprising the vector.

Applicants submit that a rejection of claims under U.S.C. §102(b) requires that the prior art reference disclose every element of the claim. It is axiomatic that there must be no differences between the subject matter of the claim and the disclosure of the prior art. The absence from the reference of any claimed element negates anticipation. Kloster Speedsteel AB v. Crucibile Inc., 793 F2d 1565, 1571, 230 U.S.P.Q. 81, 84 (Fed. Cir. 1986).

Applicants further submit that none of the cited references teach or disclose a Sertoli cell comprising a vector which functions in a Sertoli cell operatively linked to a coding sequence

for a biological protein wherein the Sertoli cell creates an immunologically privileged site *in vivo*. Furthermore, none of the references teach or disclose a Sertoli cell isolated from a transgenic non-human animal wherein the animal comprises a vector and expresses the relevant biological protein. Sertoli cells isolated from a transgenic non-human animal generally have the heterolgous coding sequence stably integrated in the genome and are typically uniform in the expression of the heterologous biological protein. Such Sertoli cells are distinct from Sertoli cells transfected *in vitro*, as taught by the cited references, which are typically a heterogenous population of cells, and may or may not harbor the heterologous-coding sequence in the genome. Therefore, the cited references do not disclose every element of the pending claims. Accordingly, Applicants submit that the rejections of the claims under 35 U.S.C. §102 (b) are overcome and withdrawal thereof is respectfully requested.

Claims 30 and 32 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gorman et al. (EP 0 260 148 A2) in view of Meulien (U.S. 5,521,070).

The Examiner admits that Gorman et al. do not teach specifically the preparation of genetically modified Sertoli cells comprising a vector comprising a coding sequence for factor IX, or that the genetically modified Sertoli cells are isolated from a transgenic animal. However, the Examiner states that Meulien disclose a novel DNA sequence coding for factor IX or a similar protein.

Applicants respectfully submit that Gorman et al. do not teach or disclose a Sertoli cell comprising a vector which functions in a Sertoli cell operatively linked to a coding sequence for a biological protein wherein the Sertoli cell creates an immunologically privileged site *in vivo*. Furthermore, Gorman et al. do not teach or disclose a Sertoli cell isolated from a transgenic non-human animal wherein the animal comprises a vector and expresses the relevant biological

protein, which are distinct from the Sertoli cells transfected *in vitro* taught by Gorman et al., as submitted above. Applicants further respectfully submit that Meulien does not cure the deficiencies of Gorman et al. Therefore, the references alone or in combination do not teach or suggest the Sertoli cells, as presently claimed. Withdrawal of the rejection under 35 U.S.C. §103(a) as allegedly unpatentable over Gorman et al. in view of Meulien is therefore respectfully requested.

Claims 30 and 32 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gorman (EP 0 260 148 A2) in view of Ciotti et al. (*Biochemistry* 35: 10119-10124, 1996).

The Examiner admits that Gorman does not teach specifically the preparation of genetically modified Sertoli cells comprising a vector comprising a coding sequence for bilirubin UDP-glucuronosyltransferase (B-UGT), or that the genetically modified Sertoli cells are isolated from a transgenic animal. However, the Examiner states that Ciotti et al. teach vectors encoding bilirubin UDP-glucuronosyltransferase and mutants thereof, and to generate isoforms of the enzyme using the COS-1 cell expression system for their biochemical studies.

Applicants respectfully submit that Gorman et al. do not teach or disclose a Sertoli cell comprising a vector which functions in a Sertoli cell operatively linked to a coding sequence for a biological protein wherein the Sertoli cell creates an immunologically privileged site *in vivo*. Furthermore, Gorman et al. do not teach or disclose a Sertoli cell isolated from a transgenic non-human animal wherein the animal comprises a vector and expresses the relevant biological protein, which are distinct from the Sertoli cells transfected *in vitro* taught by Gorman et al., as submitted above. Applicants further respectfully submit that Ciotti et al. do not cure the deficiencies of Gorman et al. Therefore, the references alone or in combination do not teach or suggest the Sertoli cells, as presently claimed. Withdrawal of the rejection under 35 U.S.C.

§103(a) as allegedly unpatentable over Gorman et al. in view of Ciotti et al. is therefore respectfully requested.

Finally, Applicants respectfully remind the Examiner of the §1.48(a) Petition filed on August 8, 2002 to correct the Inventorship in the application. Applicants have not received any decision regarding the Petition.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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